Clinical Practice Guideline for the Management of Pneumonitis/Pneumonia in CENTCOM AOR

I. Background

A. Over two dozen cases of severe pneumonitis/pneumonia have occurred in the CENTCOM AOR since March 2003. Most have required mechanical ventilation, and two patients have died. The clinical presentation has been described as rapid onset of cough and severe dyspnea +/- fever with leukocytosis and usually no antecedent illness (prodrome). Chest radiograph (CXR) demonstrates bilateral alveolar infiltrates with or without progression to findings consistent with Acute Respiratory Disease Syndrome (ARDS). The etiology of these cases is presently unknown and is the subject of an Epidemiologic Consultative Team (EPICON) investigation.

B. A number of additional uncomplicated pneumonias have been diagnosed across the CENTCOM AOR; all of these patients have recovered. The uncomplicated pneumonias seem to fall into two distinct classes: an atypical (viral) process, and a classic lobar pneumonia. The viral process is characterized by a 1-3 day history of typical upper respiratory symptoms (URI), including malaise, fever, cough, and headache. CXR demonstrates subtle lobar or bilateral interstitial infiltrates, and CBC shows a low WBC count (< 5000/µl) and thrombocytopenia (<120K/µl). The vast majority of such cases quickly resolve. The other class is characterized by leukocytosis, fever, cough, and typical unilateral lobar alveolar infiltrates on CXR suggestive of (but not proven to be) a bacterial pneumonia. These latter cases respond well to antibiotics and recover fairly rapidly.

II. Case definition

For purposes of standardization, a case of pneumonitis/pneumonia must be confirmed by presence of infiltrates on chest radiograph (CXR). The case definition for severe pneumonitis/pneumonia includes a CXR characterized by the presence of bilateral alveolar infiltrates +/- a requirement for mechanical ventilation. The remainder of this practice guideline is directed towards the management of patients who present with severe pneumonitis/pneumonia.

III. Approach to Patients with Severe Pneumonitis/Pneumonia

The challenge confronting most clinicians is not in detecting the presence of the disease but rather in identifying its cause. This is critical to diagnose and treat the disease, but also to establish common or shared factors that indicate whether cases are related to a common exposure. Even so, in the best of medical centers, less than one-third of all pneumonias reveal a specific pathogen after extensive investigation. Establishing standardized operating procedures in the clinical and diagnostic evaluation of pneumonitis/pneumonia is important for the control of disease for a population (military units) and the effective management of an individual patient. While empiric antibiotic therapy is usually necessary even in the absence of a specific etiology, it is vital that clinical specimens be obtained to link specific pathogens to clusters of cases, to exclude common causes of pneumonitis/pneumonia, and to identify unusual pathogens.

A. History. A detailed history of each case of pneumonitis/pneumonia is required to document date of onset, duration of illness before seeking medical care, symptomatology, exposures (e.g., dust, chemicals, and smoke), MOS, work environment, and geographic location. The EPICON team has prepared a detailed questionnaire that includes a patient interview (clinical situation permitting) for each case of pneumonitis/pneumonia (uncomplicated and severe) to establish links with other cases throughout AO. Ideally, a health care worker should administer this questionnaire, i.e., interview the patient. Additional data capture forms in the EPI Data Collection Instrument are included to record

laboratory test results and radiologic findings for transfer to the Center for Health Promotion and Preventive Medicine (CHPPM) in CONUS.

B. Diagnostic work-up**.** Although definitive identification of a pathogen is often elusive, it is imperative to collect clinical specimens for epidemiologic purposes, especially when the cause of a suspected outbreak is unknown. The following recommendations are based upon medical and logistical assets available at Combat Support Hospitals (CSH) in order to minimize the logistical burden to clinical staff and to facilitate the timely transfer of specimens from the clinical laboratory to Landstuhl Regional Medical Center (LRMC) and/or CONUS. **Severe cases of pneumonitis/pneumonia, or uncomplicated cases with patterns with bilateral disease on CXR, are best managed at a centralized medical treatment facility with advanced laboratory services and the capability to perform bronchoscopic examinations. Due to the potential for rapid progression to respiratory failure, patients with bilateral infiltrates on CXR should be evacuated to LRMC immediately after the initial evaluation described below.**

1. Laboratory

    a. CBC with manual differential (numerate eosinophils)
    b. Sputum gram stain (all CSHs) and culture (MTF-specific, 28th CSH) for patients with cough characterized by productive sputum
    c. Throat swab for detection of Group A Streptococci (*S. pyogenes)* using rapid detection assay (all CSHs)
    d. Throat swab (Dacron) for viral culture—transport at 4°C to LRMC within 96 hours
    e. Urine sample for the detection of *S. pneumoniae* and *Legionella* using rapid antigen detection assay
    f. Two (2) serum separator tubes for serologic tests—transport at 4°C with patient to LRMC or ship to address below:

        SFC Lavon Harbor
        OIF Pneumonia Lab Specimen Manager
        Division of Military Casualty Research, Room 1N-82
        Walter Reed Army Institute of Research
        503 Robert Grant Avenue
        Silver Spring, MD 20910-7500

2. Radiology. PA/LAT CXR documenting unilateral vs. bilateral disease, interstitial vs. alveolar pattern, and specific lobes involved

IV. Treatment and Case Management

A. Prognostic indicators to predict uncomplicated limited disease vs. progression to severe disease. Unfortunately, there are no good predictors to identify those patients who will progress to severe disease requiring mechanical ventilation or to distinguish between those who have bacterial versus viral infection. However, normal mental status, pulse <125 beats/minute, respiratory rate <24/minute, systolic blood pressure >90 mmHg, temperature >35°C and <40°C, and a “not very sick” appearance are fairly good predictors for outpatient therapy.

B. Fluid management of patients with severe pneumonitis/pneumonia. Many patients with severe disease have some degree of volume depletion, and adequate fluid replacement is essential. Replacement of fluids and electrolytes with normal saline or D5NS is recommended, the amount and rate carefully titrated to the patient’s clinical condition so as to avoid exacerbating pulmonary leakage and pulmonary edema. Health care providers should avoid using Lactated Ringer’s Solution, especially older racemic mixtures of Ringer’s lactate.

C. Strategies for treatment of pneumonitis/pneumonia

1. Uncomplicated pneumonitis/pneumonia. The empiric treatment of uncomplicated pneumonia using oral antibiotics such as Azithromycin (Zithromax) or Levofloxacin is common practice and often effective. Depending on the patient's clinical status, the physician may elect to initiate intravenous therapy followed by changeover to oral therapy when possible. It is imperative that combination broad-spectrum antibiotics be avoided in patients with uncomplicated pneumonia to prevent emergence of multi-drug resistant organisms.

2. Severe pneumonitis/pneumonia. Without a definitive microbiologic diagnosis, combination antibiotic therapy administered intravenously is frequently required as empiric treatment:

3rd generation cephalosporin (ceftriaxone, cefotaxime)

AND

Respiratory tract quinolone (levofloxacin (500-750 mg IV qd) >> preferred over ciprofloxacin) **OR** *Azithromycin (500 mg IV qd*)

AND

Doxycycline (100 mg IV bid)

Doxycycline is included because at least one patient had very high titers to *Coxiella* (causative agent of Q fever). There is no strong recommendation for the addition of imipenem to the above regimen. However, if imipenam is used in a seriously ill patient requiring mechanical ventilation, this should be used as a substitute for the cephalosporin.

3. Use of steroids. This clinical practice guideline neither recommends nor prohibits the use of steroids for patients with severe pneumonitis/pneumonia. The use of steroids is NOT the standard of care for management of pneumonia or ARDS in the United States. However, under certain clinical conditions and depending upon the available laboratory data, the physician may elect to give steroids (in addition to broad spectrum antibiotics) to the severely ill patient who is being mechanically ventilated. This may be appropriate in those cases where acute eosinophilic pneumonia (AEP) has been diagnosed or there is a strong clinical suspicion that the patient has AEP.

4. Pressure-control ventilation. The lone pulmonologist in theater at the 28th CSH (Baghdad) has requested that a pressure-control ventilator be placed in theater at a central referral facility (28th CSH, Baghdad) for the management of patients with severe pneumonia who may require prolonged care in theater prior to medical evacuation. The use of such a ventilator should be done by those experienced in its use. The advantages include proper management of patients that typically require high PEEP (>10) with high peak pressures (45-50) to maintain adequate oxygenation.

5. Evacuation from theater. **The clinical course of patients with severe pneumonitis/pneumonia requires immediate evacuation from theater** (dependent upon the stability of the patient for transport). This is critical because 1) most of these patients will require management in an ICU for > 7 days; 2) the diagnostic work-up requires early bronchoscopy and detailed analysis of BAL fluid; and 3) the nature of the epidemiologic investigation requires sophisticated laboratory testing and specimen collection methods not routinely available in theater. Upon evacuation, the following items should accompany the patient to LRMC: all medical notes, lab results, radiographs, and other clinical records; at least two serum separators of acute blood (transport on ice); the patient's uniform(s) and any other equipment he/she may have been wearing; all medications the patient may have been taking, including OTC; all cigarettes and other tobacco products in the patient's possession; and any other personal effects that can be acquired.